REMARKS

Claims 6, 9 and 12-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 6, 12 and 13, the Office indicates that it is unclear what is meant by the recitation "composition ... which is an injection." Claims 6, 12 and 13 have been amended to replace the phrase "which is an injection" with the phrase --wherein the composition is in an injection form--. The amendments are believed to overcome the 35 U.S.C. 112, second paragraph, rejection as it applies to claims 6, 12 and 13.

The position of the Office regarding claim 9 is that it recites a process but does not recite any process steps. Applicants respectfully submit that claim 9 as originally presented recites six process steps and that each step by itself is a process for production of the liposome of claim 1.

Notwithstanding that original claim 9 is believed to be definite, claim 9 has been amended to precisely recite a process for the production of the liposome of claim 1 comprising the step of (A), (B), (C), (D), (E) or (F). Additionally, steps (A) and (B) of claim 9 have been amended to recite that 1,2-distearol-sn-

glycero-3-phosphoethanolamine bonded to a polyalkylene glycol (PEG-DSPE) is added as a constituent lipid. This amendment is based on the description on page 17, lines 14 to 17, and Methods 1 and 2 of Working Example 1 (page 34, line 21 to page 37, lines 20, and Figs. 2 and 3) of the specification of the present application.

Removal of the 35 U.S.C. 112, second paragraph, rejections of the claims is believed to be in order and is respectfully requested.

Prior to discussing the prior art rejections of the claims, applicants note that claim 1 has been amended to recite a liposome selected from the group consisting of:

(a) a liposome to which each of a polyalkylene glycol and a non-modified serum albumin is bonded, wherein the non-modified serum albumin is bonded to the liposome via a reactive intervening group (supported, for example, by the description on page 16, lines 1 to 3, page 19, lines 13 to 19, Working Example 1 and Figs. 2 and 3);

(b) a liposome to which a serum albumin is bonded via a polyalkylene glycol, wherein the serum albumin is bonded to the polyalkylene glycol via a reactive intervening group (supported, for example, by the description on page 16, lines 4 to 8, page 21,

lines 16 to 21, page 22, lines 17 to 21, Working Example 2 and Figs. 4 and 5); and

(c) a liposome wherein the liposome and a polyalkylene glycol are bonded to a serum albumin via reactive intervening groups at a different site (supported, for example, by the description on page 16, lines 8 to 12, page 24, lines 5 to 9, Working Example 3 and Figs. 6 and 7).

New claims 14 to 16 have been added to the application. Claim 14 is supported, for example, by the description on page 16, lines 20 to 28, page 19, lines 13 to 19, page 21, lines 4 to 6, Working Example 1 and Figs. 2 and 3. Claim 15 is supported, for example, by the description on page 16, lines 4 to 8, page 21, lines 7 to 21, page 22, lines 17 to 21, Working Example 2 and Figs. 4 and 5. Claim 16 is supported, for example, by the description on page 16, lines 8 to 12, page 23, line 26 to page 24, line 9, page 25, lines 3 to 6, Working Example 3 and Figs. 6 and 7.

Claims 1-2, 5-6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Kamps et al. (*Biochimica et Biophysica Acta* 1278 (1996); hereinafter "Kamps").

Kamps teaches the preparation of conjugates of (modified) human serum albumin and liposomes: drug carriers with an intrinsic anti-HIV activity. Specifically, Kamps discloses that cis-aconitic

anhydride modified human serum albumin (Aco-HSA) is used to liposome conjugates. Kamps also teaches native HSA-liposomes. However Kamps neither discloses nor suggests a non-modified human serum albumin (non-modified HSA)-PEG-liposome.

In Kamps, serum albumin is not used. Kamps teaches PEG-liposomes to which Aco39-HSA or Aco53-HSA is bonded, and diameters of these liposomes are compared. Further, Kamps teaches the disappearance of control PEG-DSPE-liposomes (•), Aco39-HSA-PEG-liposomes (◦) and Aco-53-HSA-PEG-liposomes (▲) in rat serum (Fig. 3). Here, Aco39HSA-PEG-liposomes (◦) and Aco53-HSA-PEG-liposomes (▲) are eliminated from rat serum at a rate faster than that observed for control PEG-DSPE-liposomes (•).

However, in the present invention, the concentration (•) of an rHSA-PEG-modified liposome in blood is higher than that of a PEG-modified liposome (♦), with lapse of time (Fig. 1). Please note that the control PEG-DSPE-liposomes (•) of Kamps is the same as the PEG-modified liposome in the present application.

Therefore, PEG-rHSA-modified liposome according to the present invention is distinguished from the modified liposomes of Kamps in blood level.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Panagi et al. (*International Journal of Pharmaceutics*, 1999; hereinafter "Panagi").

Panagi teaches *in vitro* binding (only incubating for one hour) of HSA, IgG, and HDL on liposomes of different composition and correlation with the BLOOD/RES ratio of liposomes. Specifically, *in vitro* binding of the human serum albumin (HSA) on unilamellar liposomes of different lipid composition was studied in Panagi. The unilamellar liposomes of Panagi comprises poly(ehtyleneglycol)-distearoylphosphatidylethanolamine (DSP-PEG) in their membranes. In Panagi, HSA is not bonded to the unilamellar liposome via a reactive intervening group. Therefore, the liposomes of the present application are distinct from those of Panagi.

Claims 1-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Tardi et al. (*J. Immunological Methods*, 1997; hereinatfer "Tardi").

Tardi teaches an immune response to ovalbumin covalently coupled to liposomes is prevented when the liposomes used contain doxorubicin. Specifically, highly immunogenic protein ovalbumin is conjugated onto liposomes composed of DSPC/Chol with PEG-DSPE to prevent liposome aggregation and to engender increased circulation lifetimes (abstract). In Tardi, ovalbumin is used as albumin, and

not serum albumin as is used in the present application. Therefore, the liposomes of the present application are distinct from those of Tardi.

In Fig. 1 of Tardi, ovalbumin-coated 2% PEG liposomes (•) are eliminated from the circulation at a rate faster than that observed for 2% PEG liposomes (▪). However, in the present invention , the concentration (•) of a PEG-rHSA-modified liposome in blood is higher than that of a PEG-modified liposome (♦), with lapse of time (Fig. 1).

Removal of the 35 U.S.C. 102(b) rejections of the claims is believed to be in order and is respectfully requested.

Finally, applicants note that a related CIP application of PCT/JP2003/014405, U.S. Application Serial No. 11/078,502, is pending and is being examined by the Examiner in charge of the present application.

The foregoing is believed to be a complete and proper response to the Office Action dated October 23, 2007, and is believed to place this application in condition for allowance. If, however, minor issues remain that can be resolved by means of a telephone interview, the Examiner is respectfully requested to contact the undersigned attorney at the telephone number indicated below.

PATENT APPLN. NO. 10/534,874 **PATENT**
RESPONSE UNDER 37 C.F.R. §1.111 **NON-FINAL**

In the event that this paper is not considered to be timely filed, applicants hereby petition for an appropriate extension of time. The fee for any such extension may be charged to our Deposit Account No. 111833.

In the event any additional fees are required, please also charge our Deposit Account No. 111833.

Respectfully submitted,

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